

CLAIMS

WHAT IS CLAIMED IS:

1. An in vitro method of capturing one or more target simple sequence repeats, wherein the method comprises the steps of:

5 providing one or more modified oligonucleotide conjugates, wherein each of the modified oligonucleotide conjugates comprises at least one locked nucleic acid and a linking molecule;

incubating a sample of nucleic acids with the modified oligonucleotide conjugates, thereby forming one or more hybridized duplexes, wherein each duplex comprises a target simple sequence repeat portion and a modified oligonucleotide conjugate portion;

contacting substantially all of the hybridized duplexes with a linking source, such that the linking molecule of each duplex that contacts the linking source forms a bond with the linking source; and

separating substantially all of the hybridized duplexes from the sample of nucleic acids by extracting the linking source from the sample.

2. The method of claim 1, wherein the sample of nucleic acids contains one or more nucleic acid molecules having a nucleotide sequence which comprises one or more target simple sequence repeats.

20 3. The method of claim 1, wherein the captured simple sequence repeat portion comprises 1, 2, 3, or 4 base repeats.

4. The method of claim 1, further comprising the step of disassociating the targeted simple sequence repeat portion of each of the hybridized duplexes from the linking source and modified oligonucleotide conjugate.

5. The method of claim 4, wherein the disassociating step further comprises incubating the hybridized duplexes with an alkaline buffer, such that the targeted simple sequence repeat portion is disassociated from the modified oligonucleotide conjugate and the linking source.

6. The method of claim 5, wherein the alkaline buffer has a pH between 9 and 10.

7. The method of claim 1, wherein the incubating step comprises using reaction conditions at which substantially all of the targeted simple sequence repeats form a strand displacing "A" helix with the modified oligonucleotide conjugates.

8. The method of claim 1, wherein the method forms a new library enriched in the targeted simple sequence repeat or repeats.

9. A library enriched with targeted simple sequence repeats, formed by the method of claim 1.

10. The library according to claim 9, wherein the targeted simple sequence repeats comprise 1, 2, 3, or 4 base repeats.

11. The method of claim 1, wherein the simple sequence repeat portion of the hybridized duplex is a portion of the insert in the 3.5 kb clone.

12. The method of claim 1, further comprising the step of obtaining the sample of simple sequence repeats from a plasmid library.

13. The method of claim 12, wherein at least one of the one or more plasmids is a circular plasmid.

14. The method of claim 1, further comprising the step of obtaining the sample of simple sequence repeats from a double stranded DNA plasmid library.

5 15. The method of claim 1, further comprising the step of obtaining the sample of simple sequence repeats from DNA sequences.

16. The method of claim 1, further comprising the step of obtaining the sample of simple sequence repeats from genomic DNA.

17. The method of claim 1, further comprising the step of obtaining the sample of simple sequence repeats from RNA sequences.

18. The method of claim 1, wherein the modified oligonucleotides comprise nucleotide sequences that are complementary to the target simple sequence repeats.

19. The method of claim 1, wherein the linking molecule comprises biotin bound to a 5' end of the modified oligonucleotide.

20. The method of claim 1, wherein the linking molecule comprises an antibody, biotin, immunoglobulin, or carbohydrate.

21. The method of claim 1, wherein the linking source comprises streptavidin-coated beads.

20 22. The method of claim 1, wherein the linking source comprises an antigen, avidin, protein A, or lectin.

23. The method of claim 1, wherein the separating step comprises using a magnet to extract the linking source and hybridized duplexes from the sample of simple sequence repeats.

24. An in vitro method of capturing one or more target simple sequence repeats, wherein the method comprises the steps of:

providing one or more modified oligonucleotide conjugates, wherein each of the modified oligonucleotide conjugates comprises at least one locked nucleic acid and
5 a linking molecule;

incubating a sample of nucleic acids with the modified oligonucleotide conjugates, thereby forming one or more hybridized duplexes, wherein each duplex comprises a target simple sequence repeat portion and a modified oligonucleotide conjugate portion:

binding the linking molecule biotin on the modified oligonucleotides to streptavidin on coated magnetic beads, such that the magnetic beads are linked to the hybridization duplexes;

separating the hybridized duplexes from other materials with a magnet;

washing the hybridized duplexes;

incubating the hybridized duplexes with buffer of pH of about 9.5 such that the targeted simple sequence repeat dissociates from the modified oligonucleotide conjugate and the magnetic bead;

transforming the simple sequence repeats in E coli; and

sequencing the transformed simple sequence repeats.

20 25. A hybridized duplex comprising:

a locked nucleic acid portion, and

a simple sequence repeat portion.

26. The hybridized duplex of claim 25, further comprising a linking source.

27. A strand displacement method of capturing target nucleic acids, wherein the improvement comprises using one or more target nucleic acid molecules having a nucleotide sequence which comprises one or more simple sequence repeats.

28. A kit for capturing target simple sequence repeats, comprising:

5 one or more modified oligonucleotide conjugates, wherein each of the modified oligonucleotide conjugates comprises at least one locked nucleic acid and a linking molecule.

a hybridized duplex comprised of a simple sequence repeat portion and a modified oligonucleotide conjugate portion;

10 a linking source, wherein the linking source is attachable to the linking molecule of the modified oligonucleotide conjugate; and

15 a means for separating the hybridized duplexes from a sample of nucleic acids.

29. The kit of claim 28, further comprising an alkaline buffer.

30. The kit of claim 28, wherein the buffer has a pH between 9 and 10.